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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER	
WOODWARD, CHERIE MICHELLE	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 08/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/775,856	RADEMACHER ET AL.	
	Examiner	Art Unit	
	Cherie M. Woodward	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-2, 4-12, 14-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-12, 14-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicant's Response and Amendments, filed 25 March 2004, are acknowledged. Claims 1-2, 4-12, and 14-20 are pending and under examination.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Indication of Allowability Withdrawn

3. The indicated allowability of claim 10, but for its dependence on a rejected independent claim is withdrawn in view of the art previously cited over claims 1-2 and 5-9. Rejections based on the newly cited references follow.

Claim Objections/Rejections Withdrawn

Claim Rejections - 35 USC § 112, First Paragraph

Written Description

3. The rejection of claims 1-2, 4-12, and 14-20 under 35 USC 112, first paragraph, written description for the generic terminology "A-type cyclitol-containing carbohydrate substance containing a Zn2+ ion" is withdrawn in light of Applicant's amendments to the claims. However, new written description rejections are set forth below.

4. The rejection of claim 4 under 35 USC 103(a) as being unpatentable over Huang et al., (Endocrinology 1993; 132:652-57) is withdrawn. Applicant's arguments with respect to the rejection have been considered but are moot in view of the new grounds of rejection.

Claims Objections/Rejections Maintained

Claim Rejections - 35 USC § 102(b)

5. The rejection of claims 1-2, and 5-9 under 35 USC 102(b) as being anticipated by Huang et al., (Endocrinology 1993; 132:652-57), are maintained for the reasons of record in the Office Action of 27 October 2003 and for the reasons set forth herein.

The claims are drawn to a genus of monoclonal antibodies against an A-type inositolphosphoglycan (IPG) substance, a pharmaceutical composition comprising the claimed antibodies, and an immunoassay.

Applicant argues that Huang et al., discloses polyclonal antibodies raised against variable surface glycoproteins from *Trypanosome brucei* and that because these antibodies are polyclonal, they do not anticipate the instant claims to a monoclonal antibody. Applicant's arguments filed 25 March 2004 have been fully considered but they are not persuasive.

Applicant is correct in stating that differences in monoclonal and polyclonal antibodies are well known in the art. What Applicant fails to appreciate is that polyclonal antibodies are compositions of a multiplicity of monoclonal antibodies, each specific to a particular antigenic epitope. It is well established that individual B-cells produce antibodies to only one antigenic epitope and that once programmed, a B-cell can only make antibodies to against the programmed epitope. Because a full complement of B-cells are involved in eliciting a cellular immune response to an antigen via immunization, for example, antibodies against many different antigenic epitopes will be produced by the numerous B-cells involved in the cellular immune response. Monoclonal antibodies are isolated by fusing the multiplicity of B-cells with myelomas (usually) to immortalize them, thereby creating hybridomas. A screening process takes place that permits identification of particular hybridoma with particular antigenic epitopes (see, for exemplary purposes only, Harlowe et al., Antibodies-A Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988 pp. 92, 141-142, and 148). The Examiner acknowledges that the process of creating monoclonal antibodies is well known in the art and is considered routine experimentation.

Applicant's claims are drawn to a genus of monoclonal antibodies against an A-type inositolphosphoglycan (IPG) substance. There is no disclosure in the claims or the specification that teaches the specific type-A IPG epitopes that the claimed antibodies are drawn to. The specification disclosed three antibody cell lines designated 2D1, 5HG, and 2P7 (see p. 30). However, these specific cell lines are not claimed. Rather, the claims are drawn to a genera of monoclonal antibodies. This lack of specificity in claiming Applicant's invention permits the rejection over Huang et al., because Huang et al., teach the polyclonal antiserum comprising a multiplicity of individual monoclonal antibodies which, in fact, bind to A-type inositolphosphoglycan (IPGs). In Applicant's Remarks (p. 7, first paragraph), Applicant's state that the polyclonal antibodies disclosed by Huang et al., are specific for the GPI anchor of the variable surface glycoproteins and that they cross-react with IPGs. Thus, Applicants acknowledge that the antibodies of Huang et al., bind the recited type A-IPGs.

Absent evidence to the contrary, such as a claim to a specific monoclonal antibody with a defined epitope, evidence of biological deposit, such that the skilled artisan would be aware of the epitope specificity of the specifically claimed antibody, or the disclosure of an amino acid or nucleotide sequence such that the skilled artisan would be apprised of the structure and function of the specifically claimed recombinant monoclonal antibody, Huang et al., teach the invention of claims 1-2 and 5-9, as written.

New Claim Objections/Rejections

Claim Rejections - 35 USC § 112, First Paragraph

Enablement

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-2, 4-12, and 14-20 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Specific antigenic epitopes of the claimed genus of monoclonal antibodies, monoclonal antibody deposit information, recombinant antibody amino acid or nucleic acid sequences, critical or essential to the practice of the invention, but not included in the claims is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

The claims are drawn to a monoclonal antibody that specifically binds to an isolated A-type substance obtainable from human liver or placenta, wherein the substance is an A-type inositolphosphoglycan (IPG) substance that has a biological activity of regulating lipogenic activity and inhibiting cAMP dependent protein kinase; wherein the substance comprises phosphate; a pharmaceutical composition comprising the monoclonal antibody of claim 1; wherein the monoclonal antibody is an antagonist having one or more of the recited properties; wherein the monoclonal antibody is linked to a label; wherein the monoclonal antibody is immobilized on a solid phase; an immunoassay method comprising contacting a biological sample with the monoclonal antibody of claim 1 under suitable conditions for specific binding of the monoclonal antibody to an A-type substance present in the sample, if any, and determining whether the monoclonal antibody binds specifically to the sample; additionally comprising measuring the amount of specific binding as an indication of the concentration of the A-type substance in the sample; additionally comprising determining the concentration of one or more P-type IPGs and then determining the ratio of the concentration of P-type IPGs to the concentration of A-type substance determined in the immunoassay method; a monoclonal antibody that specifically binds to an A-

type IPG wherein the substance has a biological activity of regulating lipogenic activity and inhibiting cAMP dependent protein kinase and a molecular weight determined using negative mode MALDI mass spectroscopy or a molecular weight determined using positive mode MALDI mass spectroscopy; wherein the substance comprises phosphate; a pharmaceutical composition comprising the monoclonal antibody of claim 11 in combination with a pharmaceutically acceptable carrier; wherein the monoclonal antibody is an antagonist having the recited properties; wherein the monoclonal antibody is linked to a label; wherein the monoclonal antibody is immobilized on a solid phase; an immunoassay method comprising contacting a biological sample with the monoclonal antibody of claim 11 under suitable conditions for specific binding of the monoclonal antibody to an A-type substance present in the sample, if any, and determining whether the monoclonal antibody binds specifically to the sample; additionally comprising measuring the amount of specific binding as an indication of the concentration of the A-type substance in the sample; additionally comprising determining the concentration of one or more P-type IPGs and then determining the ratio of the concentration of P-type IPGs to the concentration of A-type substance determined in the immunoassay method.

The specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description; or (3) deposited in compliance with the criteria set forth in 37 CFR §§1.801-1.809. It is unclear whether cell lines which produce the antibodies having the exact chemical identity and properties of the antibodies designated 2D1, 5HG, and 2P7 (see p. 30 of the specification) have been deposited with and public depository, such that they are known and publicly available, or can be reproducibly isolated without undue experimentation. Accordingly, filing evidence of reproducible production of the cell lines and antibodies necessary to practice the instant invention or filing of evidence of deposit is required. Without a publicly available deposit of the above-mentioned cell lines, one of skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the cell lines which produce the chemically and functionally distinct antibodies claimed, and/or the amino acid or nucleic acid sequence of the claimed antibodies are unpredictable events. For example, very different V_H chains can combine with the same V_L chain to produce antibody binding sites with nearly the same, size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_L sequences to produce antibodies with very similar properties. These observations indicate that divergent variable region sequences, both in and out of complementarity determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics.

Therefore, it would require undue experimentation to reproduce the monoclonal antibodies as produced by the 2D1, 5HG, and 2P7 cell lines recited on p. 30 of the specification.

Further, the specification does not reasonably teach how to make or use every monoclonal antibody population specific for type-A inositolphosphoglycans (IPGs). The specification discusses the antibody cell lines designated 2D1, 5HG, and 2P7 (p. 30), but nothing substantial is known about these cell lines and no deposit information is provided such that the skilled artisan could compare the antibodies of the cells lines discussed in the disclosure to any other known antibody. Applicant mentions the cell lines designated 2D1, 5HG, and 2P7, but provides no guidance as to what modifications or structure are important for the predictable function of the antibodies produced by those cell lines or for any other monospecific antibody. Very different structures may be found on antibodies with the same specificity, as noted above. Conversely, similar structure may be found on antibodies having different specificities. Moreover, the different "types" of IPGs known in the art appear to define groups of IPGs with similar biological activities, but which differ structurally within the group in unknown fashion. It is not clear what structure of the antigen is required for function in the invention nor would one know based on a competitive binding assay determination whether an identical structure or epitope were being bound. In the instant case, the interrelationships of the properties of the three disclosed antibodies are not clear. It is not clear whether the disclosed antibodies bind to similar members within the structurally diverse populations of IPGs which are grouped on the basis of similar biological activities or if the different antibodies bind to a similar or cross-reactive epitope.

Due to the large quantity of experimentation necessary to determine what modifications or structure are important for the predictable function of any of the claimed monospecific antibodies, such that it can be determined how to make and use the claimed antibodies, the lack of direction/guidance presented in the specification regarding same, the lack of sufficient working examples directed to same, the complex nature of the invention, the state of the prior art establishing that monoclonal antibodies are not predictably reproduced, and the breadth of the claims which fail to recite any particular monoclonal antibody, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, First Paragraph

Written Description/Failure to Deposit

8. Claims 1-2, 4-12, and 14-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to a monoclonal antibody that specifically binds to an isolated A-type substance obtainable from human liver or placenta, wherein the substance is an A-type inositolphosphoglycan (IPG) substance that has a biological activity of regulating lipogenic activity and inhibiting cAMP dependent protein kinase; wherein the substance comprises phosphate; a pharmaceutical composition comprising the monoclonal antibody of claim 1; wherein the monoclonal antibody is an antagonist having one or more of the recited properties; wherein the monoclonal antibody is linked to a label; wherein the monoclonal antibody is immobilized on a solid phase; an immunoassay method comprising contacting a biological sample with the monoclonal antibody of claim 1 under suitable conditions for specific binding of the monoclonal antibody to an A-type substance present in the sample, if any, and determining whether the monoclonal antibody binds specifically to the sample; additionally comprising measuring the amount of specific binding as an indication of the concentration of the A-type substance in the sample; additionally comprising determining the concentration of one or more P-type IPGs and then determining the ratio of the concentration of P-type IPGs to the concentration of A-type substance determined in the immunoassay method; a monoclonal antibody that specifically binds to an A-type IPG wherein the substance has a biological activity of regulating lipogenic activity and inhibiting cAMP dependent protein kinase and a molecular weight determined using negative mode MALDI mass spectroscopy or a molecular weight determined using positive mode MALDI mass spectroscopy; wherein the substance comprises phosphate; a pharmaceutical composition comprising the monoclonal antibody of claim 11 in combination with a pharmaceutically acceptable carrier; wherein the monoclonal antibody is an antagonist having the recited properties; wherein the monoclonal antibody is linked to a label; wherein the monoclonal antibody is immobilized on a solid phase; an immunoassay method comprising contacting a biological sample with the monoclonal antibody of claim 11 under suitable conditions for specific binding of the monoclonal antibody to an A-type substance present in the sample, if any, and determining whether the monoclonal antibody binds specifically to the sample; additionally comprising measuring the amount of specific binding as an indication of the concentration of the A-type substance in the sample; additionally comprising determining the concentration of one or more P-type IPGs and then determining

the ratio of the concentration of P-type IPGs to the concentration of A-type substance determined in the immunoassay method.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117).

The specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description; or (3) deposited in compliance with the criteria set forth in 37 CFR §§1.801-1.809. It is unclear whether cell lines which produce the antibodies having the exact chemical identity and properties of the antibodies designated 2D1, 5HG, and 2P7 (see p. 30 of the specification) have been deposited with and public depository, such that they are known and publicly available, or can be reproducibly isolated without undue experimentation. Accordingly, filing evidence of reproducible production of the cell lines and antibodies necessary to practice the instant invention or filing of evidence of deposit is required. Without a publicly available deposit of the above-mentioned cell lines, one of skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the cell lines which produce the chemically and functionally distinct antibodies claimed, and/or the amino acid or nucleic acid sequence of the claimed antibodies are unpredictable events. For example, very different V_H chains can combine with the same V_L chain to produce antibody binding sites with nearly the same, size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_L sequences to produce antibodies with very similar properties. These observations indicate that divergent variable region sequences, both in and out of complementarity determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Therefore, it would require undue experimentation to reproduce the monoclonal antibodies as produced by the 2D1, 5HG, and 2P7 cell lines recited on p. 30 of the specification.

To provide adequate written description and evidence of possession of a claimed genus of monoclonal antibodies against an A-type inositolphosphoglycan (IPG) substance, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the

members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states, "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

No specific species of the claimed genus of monoclonal antibodies against an A-type inositolphosphoglycan (IPG) substance are disclosed that are within the scope of the claimed genus. The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claim encompasses numerous species that are not further described.

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is a therapeutic agent, a reference molecule, and a therapeutic index. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

9. Furthermore, unless the deposit was made at or before the time of filing, a declaration filed under the 37 C.F.R. 1.132 is necessary to construct a chain of custody. The declaration, executed by a person in a position to know, should identify the deposited monoclonal antibodies by their depository accession number, establish that the deposited monoclonal antibodies are the same as that described in the specification, and establish that the deposited monoclonal antibodies were in Applicant's possession at the time of filing. See In re Lundak, 773 F.2d. 1216, 227 U.S.P.?Q. 90 (Fed. Cir. 1985).

It is not clear from the disclosure that deposits of the claimed monoclonal antibodies have been made or that their deposit, if done, meets all the criteria set forth in MPEP 608.01(p)(C), items 1-3.

Assurance of compliance may be in the form of a declaration or averment under oath. A suggested format for such a declaration or averment is outlined below:

SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL

A declaration by applicant, assignee, or applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection and rejection based on a lack of availability of biological material.

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restrictions on the availability to the public of the material will be irrevocably removed upon the granting of a patent.

5. States that the material has been deposited under conditions that ensure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 35 CFR 1.14 and 35 USC 122.

6. States that the deposited material will be stored with all care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case at least thirty (30) years after the date of a deposit or for the enforceable life of the patent, whichever is longer.

7. Acknowledges the duty to replace the deposit should the depository be unable to furnish a sample when requested due to the condition of the deposit.

8. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, name and address of the depository, and the complete taxonomic description.

As a possible means of completing the record, applicants may submit a copy of the deposit receipt.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (f) he did not himself invent the subject matter sought to be patented.

11. Claims 1-2, 4-12, and 14-20 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

Application 09/254,745, now US Patent 6,495,330, the filing under 35 USC 371 of PCT/GB97/02533 published as WO 98/10791 and Application 09/254,800, now US Patent 6,716,592, the filing under 35 USC 371 of PCT/GB97/02440 published as WO 98/11435 have an inventive entity that is different from that of the instant application. These references disclose the instant claimed monoclonal antibodies (pp. 13-16), immunoassays, and methods using labeled immobilized antibodies to capture/isolate and measure IPGs (pp. 7-8). Further, both specifications appear to be largely identical to the instant disclosure. See MPEP 2137.

12. Claims 11-12 and 15-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Huang et al., (Endocrinology 1993; 132:652-57) (previously cited in the Office Action of 27 October 2003 and *supra*).

The claims recite a monoclonal antibody that specifically binds to an isolated A-type substance obtainable from human liver or placenta, wherein the substance is an A-type inositolphosphoglycan (IPG) substance that has a biological activity of regulating lipogenic activity and inhibiting cAMP dependent protein kinase; wherein the substance comprises phosphate; a pharmaceutical composition comprising the monoclonal antibody of claim 1; wherein the monoclonal antibody is an antagonist having one or more of the recited properties; wherein the monoclonal antibody is linked to a label; wherein the monoclonal antibody is immobilized on a solid phase; an immunoassay method comprising contacting a biological sample with the monoclonal antibody of claim 1 under suitable conditions for specific binding of the

monoclonal antibody to an A-type substance present in the sample, if any, and determining whether the monoclonal antibody binds specifically to the sample; additionally comprising measuring the amount of specific binding as an indication of the concentration of the A-type substance in the sample; additionally comprising determining the concentration of one or more P-type IPGs and then determining the ratio of the concentration of P-type IPGs to the concentration of A-type substance determined in the immunoassay method; a monoclonal antibody that specifically binds to an A-type IPG wherein the substance has a biological activity of regulating lipogenic activity and inhibiting cAMP dependent protein kinase and a molecular weight determined using negative mode MALDI mass spectroscopy or a molecular weight determined using positive mode MALDI mass spectroscopy; wherein the substance comprises phosphate; a pharmaceutical composition comprising the monoclonal antibody of claim 11 in combination with a pharmaceutically acceptable carrier; wherein the monoclonal antibody is an antagonist having the recited properties; wherein the monoclonal antibody is linked to a label; wherein the monoclonal antibody is immobilized on a solid phase; an immunoassay method comprising contacting a biological sample with the monoclonal antibody of claim 11 under suitable conditions for specific binding of the monoclonal antibody to an A-type substance present in the sample, if any, and determining whether the monoclonal antibody binds specifically to the sample; additionally comprising measuring the amount of specific binding as an indication of the concentration of the A-type substance in the sample; additionally comprising determining the concentration of one or more P-type IPGs and then determining the ratio of the concentration of P-type IPGs to the concentration of A-type substance determined in the immunoassay method.

Huang et al., teach as stated in the Office Action of 27 October 2003 and *supra*. In summary, Huang et al., teach the isolation of inositolphosphoglycan insulin mediators and the use of polyclonal antibodies which bind to the mediators in assays thereby inhibiting the activities of the mediators (see e.g. p. 654).

As stated *supra*, Applicant's claims are drawn to a genus of monoclonal antibodies against an A-type inositolphosphoglycan (IPG) substance. There is no disclosure in the claims or the specification that teaches the IPG epitopes that the claimed antibodies are drawn to. This lack of specificity in claiming Applicant's invention permits the rejection over Huang et al., because Huang et al., teach the polyclonal antiserum comprising a multiplicity of individual monoclonal antibodies which, in fact, bind to A-type inositolphosphoglycan (IPGs). Absent evidence to the contrary, such as a claim to a specific monoclonal antibody, evidence of biological deposit, such that the skilled artisan would be aware of the epitope specificity of the specifically claimed antibody, or the disclosure of an amino acid or nucleotide sequence

such that the skilled artisan would be apprised of the structure and function of the specifically claimed (in this case, recombinant) monoclonal antibody, Huang et al., teach the invention of claims 15-20, as written.

Additionally, the claims recite the measurement of an inherent physical property (molecular weight) of the substance to be bound by the antibody. A measurement of an inherent physical property is a method or process that is not properly characterized as a composition of matter, such as a monoclonal antibody. Thus, claim 11 is read as a product-by-process claim. As such, the underlying product must be allowable in order for the claim to be allowable. In this case, the underlying product, the genus of monoclonal antibodies, is rejected as being unpatentable over Huang et al. See MPEP 2113.

Claim Rejections - 35 USC § 103

13. Claims 1-2, 4-12, and 14-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al., (Endocrinology 1993; 132:652-57) (previously cited in the Office Action of 27 October 2003 and *supra*) in view of Harlowe et al., (Antibodies-A Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988 pp. 92, 141-142, 321-323, and 555-559), and further in view of Romero et al., (Proc Nat Acad Sci USA 1990 Feb; 87(4):1476-1480) and Larner US Patent 5,750,348 (12 May 1998, benefit to 8 July 1994).

The claims recite a monoclonal antibody that specifically binds to an isolated A-type substance obtainable from human liver or placenta, wherein the substance is an A-type inositolphosphoglycan (IPG) substance that has a biological activity of regulating lipogenic activity and inhibiting cAMP dependent protein kinase; wherein the substance comprises phosphate; a pharmaceutical composition comprising the monoclonal antibody of claim 1; wherein the monoclonal antibody is an antagonist having one or more of the recited properties; wherein the monoclonal antibody is linked to a label; wherein the monoclonal antibody is immobilized on a solid phase; an immunoassay method comprising contacting a biological sample with the monoclonal antibody of claim 1 under suitable conditions for specific binding of the monoclonal antibody to an A-type substance present in the sample, if any, and determining whether the monoclonal antibody binds specifically to the sample; additionally comprising measuring the amount of specific binding as an indication of the concentration of the A-type substance in the sample; additionally comprising determining the concentration of one or more P-type IPGs and then determining the ratio of the concentration of P-type IPGs to the concentration of A-type substance determined in the immunoassay method; a monoclonal antibody that specifically binds to an A-type IPG wherein the substance has a biological activity of regulating lipogenic activity and inhibiting cAMP dependent protein kinase and a

molecular weight determined using negative mode MALDI mass spectroscopy or a molecular weight determined using positive mode MALDI mass spectroscopy; wherein the substance comprises phosphate; a pharmaceutical composition comprising the monoclonal antibody of claim 11 in combination with a pharmaceutically acceptable carrier; wherein the monoclonal antibody is an antagonist having the recited properties; wherein the monoclonal antibody is linked to a label; wherein the monoclonal antibody is immobilized on a solid phase; an immunoassay method comprising contacting a biological sample with the monoclonal antibody of claim 11 under suitable conditions for specific binding of the monoclonal antibody to an A-type substance present in the sample, if any, and determining whether the monoclonal antibody binds specifically to the sample; additionally comprising measuring the amount of specific binding as an indication of the concentration of the A-type substance in the sample; additionally comprising determining the concentration of one or more P-type IPGs and then determining the ratio of the concentration of P-type IPGs to the concentration of A-type substance determined in the immunoassay method.

Huang et al., teach as stated in the Office Action of 27 October 2003, and *supra*. In summary, Huang et al., teach the isolation of inositolphosphoglycan insulin mediators and the use of polyclonal antibodies which bind to the mediators in assays thereby inhibiting the activities of the mediators (see e.g. p. 654). Huang et al., do not teach individual monoclonal antibodies against specific epitopes of the IPGs.

Harlowe et al., teach the use of polyclonal sera for hybridoma fusions to create monoclonals (p. 92 and 148). Direct and indirect labeling of antibodies are taught at p. 321-323. Immunoassays, including two-antibody sandwich assays are taugth at 555-559.

Romero et al, teach the use of anti-IPG antibodies in an ELISA assay.

Larner teaches a method for detecting insulin resistance by using both myoinositol (A-type) and chiroinositol (P-type) as indicators where the "myo/chiro ratio" is utilized to characterize insulin resistance (abstract, column 1, lines 59-67 to column 2, lines 1-2).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have elicited monoclonal antibodies to the inositolphosphoglycan mediators of Huang et al., because Huang et al., teach that the mediators are of clinical interest and that the mediators were excellent antigenic targets for the production of antibodies. It would have been *prima facie* obvious to have generated monoclonal antibodies in order to provide a potentially unlimited source of homogenous reagent for uses such as affinity purification, functional studies, or clinical studies of the macromolecules using the techniques disclosed by Harlowe et al., Romero et al., or Larner. One would have reasonably

expected success because Huang et al., teach that the structures of the IPGs are antigenic and bind antibodies elicited to a structurally similar macromolecule. Additionally, Romero et al., and Harlowe et al., provide further motivation for the labeling and solid-phase immobilization of anti-IPG antibodies in view of Huang et al., and Larner provides motivation for comparing the ratios of A-type to P-type IPGs in diagnostic immunoassays.

Additionally, the claims 11-12 recite the measurement of an inherent physical property (molecular weight) of the substance to be bound by the antibody. A measurement of an inherent physical property is a method or process that is not properly characterized as a composition of matter, such as a monoclonal antibody. Thus, claim 11 is read as a product-by-process claim. As such, the underlying product must be allowable in order for the claim to be allowable. In this case, the underlying product is rejected as being unpatentable over Huang et al. in view of See MPEP 2113.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cherie M. Woodward whose telephone number is (571) 272-3329. The examiner can normally be reached on Monday - Thursday 9:00am-7:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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CMW

AU 1647

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
AU1647

8/28/06